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EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,119	CHUNG, YIH-LIN	
	Examiner	Art Unit	
	Alicia R. Hughes	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-4,6-10,12,13 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,11 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims and Examination

Claims 1-21 are pending. However, only claims 1, 5, 11, and 14-17 are the subject of this Office Action. Claims 2-4, 6-10, 12, 13, and 18-21 are withdrawn from consideration, being drawn to a non-elected invention. See 37 C.F.R. 1.142(b).

Applicant's arguments and amendments filed on 22 June 2007 in response to the non-final rejection filed by this Office on 23 March 2007 have been fully considered, but they are not deemed to be persuasive. Rejections and objections not reiterated from previous office actions are hereby withdrawn. The following rejections are reiterated and expounded upon, and they constitute the complete set presently being applied to the instant application, hereby making this rejection FINAL.

Claim Rejections - 35 U.S.C. §112.1

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant, in its Remarks filed on 22 June 2007, amended claim 1 to define therapeutic gain such that "therapeutic gain comprises preventing radiation or chemotherapy-induced complications or sequelae of mucositis, dermatitis, ulceration, tissue necrosis, fibrosis, xerostomia, plantar-palmar syndrome, and tumorigenesis, protecting normal tissues from cell death, and promoting radiation-induced wound healing in mucositis and dermatitis." This changes the scope of the claim and originally filed and a review of specification, as filed, does not disclose the invention embodied by the present set of claims. And if the same is supported, Applicant has failed to draw attention to the page and line numbers in the specification that support its amendment.

This is a new matter rejection.

Claims 1, 5, 11, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, because no mechanism of action or data is provided to support Applicant's claim for "preventing radiation or chemotherapy-induced complications ..." Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. As a result, the effect of performing the invention by one skilled in the art would be that of undue experimentation.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1)

the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that the level of skill in cancer research is high, and the results of experiments to determine cancer recurrence or the lack thereof is unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Although the applicant has provided some working examples to support increased therapeutic gain in radiotherapy based on tumor control, the applicant has failed to disclose **any** examples or data to support prevention of the same as a result of treatment with a hyperacetylating agent.

While arguably, one of skill in the art, such as a physician or biomedical researcher with a master's degree or Ph.D. in the natural sciences, would be able to deduce results as to whether **a** treatment would result in increased therapeutic gain, the status in the art regarding prevention of cancer in general is so uncertain, because today, the causative effects of cancer is so controversial and the results so lacking in predictability, a conclusion about whether the radiation or chemotherapy-induced complications would be speculative, at best. *See generally*, Danesi, Romano et al., "Pharmacogenetic Determinants of Anti-Cancer Drug Activity and Toxicity," *TRENDS in Pharmacological Sciences*, Vol. 22, No. 8, pages 420-426 and page 420, the abstract, particularly (August 2001).[1] In consideration of the foregoing, the art of the claimed invention lacks predictability because the claim is drawn too broadly.

[1] Cited on PTO Form 892 filed on 23 March 2007.

Claim Rejections - 35 U.S.C. §112.2

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 11, and 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as modified, states that "therapeutic gain comprises ***preventing*** radiation or chemotherapy-induced complications or sequelae of mucositis, dermatitis, ulceration, tissue necrosis, fibrosis, xerostomia, plantar-palmar syndrome, and tumorigenesis, protecting normal tissues from cell death, and promoting radiation-induced wound healing in mucositis and dermatitis." Emphasis added. However, the language as written is unclear. One is uncertain as to what "preventing" modifies, because the grammar and conjunctions make unclear, whether, for example, one is preventing sequelae of mucositis and dermatitis and ulceration and tissue necrosis and fibrosis and xerostomia and plantar-palmar syndrome and tumorigenesis is one limitation where each and every element must be established to be prevented or preventing belongs with "protecting normal tissues from cell death" may be another limitation in the alternative that may be addressed or for that matter, whether "preventing" is to be read as part of that limitation.

Claim Rejections – 35 U.S.C. §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 11, and 14-16 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"].[2]

This Office's arguments from its action of 23 March 2007 are incorporated herein by reference in their entirety.

The Applicant's argument that Samid does not establish a prima facie case of obviousness, because the present invention is distinguishable due to its focus on promoting cell proliferation and survival rather than promoting cell death has been considered, but it is not deemed persuasive.

Contrary to Applicant's assertions, Samid discloses: (1) that differentiation therapy is a desirable approach to cancer intervention since neoplastic transformation is the result of defects in cellular differentiation and thus inducing tumor cells to differentiate prevents tumor progression and brings about the reversal of malignancy (Col. 2, lines 54-63); (2) the administration of phenylacetate and its pharmaceutically acceptable derivatives to prevent tumor progression and the development of malignant diseases (Col. 3, lines 1-6); and (3) a pharmaceutical composition for inhibiting abnormal cell growth and inducing differentiation in nonmalignant or malignant tumor cells (Col. 4, lines 61-63).

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to administer sodium phenylbutyrate in the manner prescribed by Samid, in combination with radiotherapy, as a method of treating various cancers.

Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"] in view of Shufeng, Z., et al., *5,6-Dimethylxanthenone-4-acetic acid (DMXAA): A New Biological Response Modifier for Cancer Therapy*, Investigational New Drugs, vol. 20, 2002, pages 281-295 [hereinafter referred to as "Shufeng, et al."].[3]

The teachings of Samid, taught in this Office's action of 23 March 2007 and *supra*, are incorporated herein by reference.

Shufeng et al teach 5,6-dimethylxanthenone-4-acetic acid (DMXAA) as an investigational anti-cancer drug and as a biological response modifier (Summary, page 281, lines 1 and 31-32). Shufeng et al also teach that while DMXAA alone does not show "striking anti-tumor activity ... preclinical studies of DMXAA-drug combinations indicate that DMXAA may have a potential role in cancer treatment when co-administered with other drugs" (Page 281, lines 31-34 and page 282, lines 1).

One of ordinary skill in the art would be motivated to combine the teachings of Samid with the teachings of Shufeng et al., because the references teach overlapping subject matter, most notably, the treatment of cancer with anti-cancer/anti-tumor agents.

In light of the foregoing, one of ordinary skill in the art would be motivated to apply the teachings of Samid and the teachings of Shufeng et al to the present invention, because DMXAA

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[2] Cited on PTO Form 892 filed on 23 March 2007.

is an anti-cancer agent/biological response modifier that when combined with radiotherapy and/or phenylacetic acid and its pharmaceutically acceptable salts and derivatives, including sodium phenylbutyrate, effectively treats various cancers. When used together, in light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art that the proliferation of cancers and their associated tumors would be treatable through the combination therapy of sodium phenylbutyrate and DMXAA with radiotherapy.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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[3] Cited on PTO Form 892 filed on 23 March 2007.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

25 September 2007

ARH

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER